ROLE OF FINE NEEDLE ASPIRATION CYTOLOGY IN DIAGNOSIS OF SOFT TISSUE TUMOURS; BENEFITS AND LIMITATIONS: A TWO YEAR RETROSPECTIVE STUDY

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ABSTRACT

BACKGROUND

Soft tissues are the nonepithelial extraskeletal connective tissues of the body, excluding supporting tissues of the internal organs, glia and hematopoietic tissues. FNAC of soft tissue swelling is becoming more popular recently because of being minimally invasive technique, relatively cheap cost and safety along with fair specificity and sensitivity.

AIM

To review the role of FNAC in diagnosing soft tissue tumours and to establish cytological criteria for the most encountered STT.

METHODS

This retrospective study was done in Department of Pathology for a period two years. A total of 4508 FNA were performed. 104 aspirations were done from soft tissue swellings. Air dried and wet fixed smears were stained with Giemsa and Papanicolaou stain respectively.

RESULTS

Among 104 STT, 86 (82.3%) were diagnosed as benign lesions while 18 cases (17.3%) were malignant. Benign lesions-17 (16.3%) patients were diagnosed as benign fibrous histiocytoma followed by ganglion cyst in 14(13.5%) cases. 13 cases (12.5%) were diagnosed as haemangioma while 9 cases (8.7%) were categorized as benign spindle cell lesion. 6 cases (5.8%) each of neurofibroma and GCT of tendon sheath were reported. 6 infants (5.8%) were diagnosed as infantile fibromatosis. 5 cases (4.7%) were reported as schwannoma. 3 cases (2.9%) each of proliferative fasciitis and nodular fasciitis were diagnosed. There were 3 cases (2.9%) reported as lymphangioma. One case (1%) was diagnosed as desmoid fibromatosis. Malignant lesions-Among them, 3 cases (2.9%) were reported as MFH. Biphasic synovial sarcoma was diagnosed in 2 patients (1.9%). 2 cases (1.9%) were reported as low grade myxoid sarcoma. 1 case (1%) was diagnosed as MPNST. GIST was diagnosed in 1(1%) patient. One (1%) of the patients presented with swelling in scapular region. This was categorized under malignant round cell tumour category. 8 cases (7.6%) were diagnosed as undifferentiated pleomorphic sarcoma.

CONCLUSION

With adequate material, FNAC has a definite role in diagnosing soft tissue tumours both benign and malignant in majority of cases with no need for histopathology except in few tumours where overlapping cytological features still remain a big limitation.

KEYWORDS

Soft Tissue, Fine Needle Aspiration Cytology, Soft Tissue Tumour.

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INTRODUCTION: Soft tissues are the nonepithelial extraskeletal connective tissues of the body, excluding supporting tissues of the internal organs, glia and hematopoietic tissues. Soft tissue tumours (STT) are generally classified according to their resemblance to the presumptive normal mesenchymal cell counterparts.[1] Based on the cytomorphological features, these lesions are categorized as spindle cell, lipomatous, myxoid, inflammatory and pleomorphic type. In cases with mixed components, the specific subtype is assigned to the predominant morphological pattern.

Soft tissue tumours are not very common. The ratio of benign to malignant STT is 100:1. The cells of origin are varying, so the diagnosis of STT is difficult at times. As a result of morphological overlap and biological heterogeneity, these tumours pose a significant diagnostic challenge.[2] Fine needle aspiration cytology (FNAC) is becoming more and more popular recently because of being minimally invasive technique, relatively cheap cost and safety with fair specificity and sensitivity for the diagnosis of new cases and in differentiating benign cases from malignant.

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STT have been diagnosed routinely by histopathology, which is considered as gold standard for their evaluation. However, in the recent times where 'needle is preceding the scalpel' and the biopsy material is getting limited, it would be prudent to discuss the role and scope of FNAC in diagnosing STT.[3,4,5]

METHODS: The aim of the present study was to evaluate the role of FNAC of soft tissue lesions. This was a retrospective study done for a period of 2 years in the Department of Pathology, by using medical records and pathology reports. A total of 104 aspirations were done (unaided and guided) from palpable soft tissue swellings of size more than 0.5 cm over a period of 2 years. Complete clinical details, examination findings, and radiological investigations of all patients were studied. The patient's consent was taken before performing the procedure. The site of puncture was marked on skin and the area was cleaned with antiseptic solution. 21 gauge needle attached to 20 mL disposable plastic syringe was inserted and 4-5 passes were made before the suction was released. The aspirate was spread on glass slides, air dried and fixed in 90% alcohol, followed by staining with May Grunwald Giemsa (MGG) and Papanicolaou stain respectively. In case of guided fine needle aspiration, the laboratory investigation Prothrombin Time Index was checked for every patient.

Inclusion Criteria: All patients with soft tissue swellings with size more than 0.5 cm, referred to the Department of Pathology were included in the study.

Exclusion Criteria:

- All cases reported to be other than STT.
- All lipomatous lesions.
- Cases without clinical details.
- Smears diluted with blood.
- Smears with inadequate cellularity.

Out of 4508 fine needle aspirations (FNA), 104 aspirations were done from soft tissue swellings. In this series, male preponderance, n=54 (51.9%) was observed as compared to females, n =50 (48.1%) [Table 1]. Main clinical presentation of these patients was swelling. Pain was observed in 20 patients. Size of swelling ranged from 0.5× 5 cm in benign lesions while 10×20 cm in malignant lesion. Majority of the swellings were solitary; however multiple swellings were observed in 6 cases. Most common site observed was lower limb n=48(46.2%) followed by upper limb n=39(37.5%) [Table 2]. Majority of the benign lesions were observed in age group 21-30 years while malignant lesions were seen in 41-50 years of age group. Patients diagnosed with malignant lesions presented mainly with short progressive history. Among 104 soft tissue lesions, 86 (82.3%) were diagnosed as benign lesions while malignant lesions were 18 cases (17.3%). Both benign and malignant cytologically diagnosed lesions have been mentioned in table 3, 9 & 10. Adequate cellularity was seen in 59 cases (56.7%) while low cellularity was observed in 45 cases (43.3%) [Table 4].

Among all the lesions, various cytomorphological features including pleomorphism, nucleoli, mitosis, necrosis was noted and has been mentioned in table 5, 6, 7, 8.

Among benign STT, 17(16.3%) cases were diagnosed as benign fibrous histiocytoma. The second most common benign lesion was observed as ganglion cyst in 14(13.5%) cases. 13 cases (12.5%) were diagnosed as haemangioma. Aspiration yielded only gush of blood. 9 cases (8.7%) were categorized as benign spindle cell lesion. 6 cases (5.8%) each of neurofibroma and giant cell tumour (GCT) of tendon sheath were reported. Soft tissue swellings diagnosed as neurofibroma were painful clinically. 6 infants (5.8%) presented with swelling in cervical region and were diagnosed as infantile fibromatosis. 5 cases (4.7%) were reported as Schwannoma. 3 cases (2.9%) each of proliferative fasciitis and nodular fasciitis were diagnosed. There were 3 cases (2.9%) reported as lymphangioma. One patient (1%) was diagnosed as desmoid fibromatosis who presented with swelling on previous low caesarean section scar.

Malignant Lesions: Out of 104 soft tissue lesions, 18 cases (17.3%) were diagnosed as malignant. 3 cases (2.9%) were reported as malignant fibrous histiocytoma. Biphasic synovial sarcoma was diagnosed in 2 patients (1.9%). Two cases (1.9%) were reported as low grade myxoid sarcoma. 1 case (1%) was diagnosed as malignant peripheral nerve sheath tumour. Gastrointestinal stromal tumour (GIST) was diagnosed in 1(1%) patient presenting with swelling in epigastric region. One (1%) of the patients presented with swelling in scapular region. This was categorized under malignant round cell tumour category with possibility of Ewing's sarcoma extended. Eight cases (7.6%) were diagnosed as undifferentiated pleomorphic sarcoma.

Sex	Frequency	Percent
Female	50	48.1
Male	54	51.9
Total	**104**	**100.0**

Table 1

Site	Frequency	Percent
Chest wall	2	1.9
Forehead	2	1.9
Infra umbilical region	1	1.0
Lower limb	48	46.2
Neck region	10	9.6
Scalp	2	1.9
Upper limb	39	37.5
Total	**104**	**100.0**

Table 2

Cytological diagnosis	Frequency	Percent
Benign spindle cell lesion	9	8.7
Benign Fibrous Histiocytoma	17	16.3
Biphasic Synovial Sarcoma	2	1.9
Desmoid fibromatosis	1	1.0
Ganglion Cyst	14	13.5
Giant Cell Tumour of tendon sheath	6	5.8

Gastro intestinal stromal tumour	1	1.0
Haemangioma	13	12.5
Infantile fibromatosis	6	5.8
Low grade Myxoid sarcoma	2	1.9
Lymphangioma	3	2.9
Malignant fibrous histiocytoma	3	2.9
Malignant peripheral nerve sheath tumour	1	1.0
Neurofibroma	6	5.8
Nodular fasciitis	3	2.9
Proliferative fasciitis	3	2.9
Malignant round cell tumour	1	1.0
Schwannoma	5	4.7
Undifferentiated pleomorphic sarcoma	8	7.6
Total	**104**	**100.0**
Table 3		

Cellularity	**Frequency**	**Percent**
Cellular	59	56.7
Low	45	43.3
Total	**104**	**100.0**
Table 4		

Pleomorphism	**Frequency**	**Percent**
High	11	10.6
Minimal	23	22.1
Moderate	12	11.5
Nil	58	55.8
Total	**104**	**100.0**
Table 5		

Nucleoli	**Frequency**	**Percent**
Nil	88	84.6
Present	16	15.4
Total	**104**	**100.0**
Table 6		

Mitosis	**Frequency**	**Percent**
Nil	88	84.6
Present	16	15.4
Total	**104**	**100.0**
Table 7		

Necrosis	**Frequency**	**Percent**
Nil	93	89.4
Present	11	10.6
Total	**104**	**100.0**
Table 8		

Benign lesions	**Frequency**	**Percent**
Benign spindle cell lesion	9	10.4
Benign Fibrous Histiocytoma	17	19.7
Desmoid fibromatosis	1	1.2
Ganglion Cyst	14	16.3
Giant Cell Tumour of tendon sheath	6	7.0
Haemangioma	13	15.1
Infantile fibromatosis	6	7.0
Lymphangioma	3	3.5
Neurofibroma	6	7.0
Nodular fasciitis	3	3.5
Proliferative fasciitis	3	3.5
Schwannoma	5	5.8
Total	86	100.0
Table 9		

Malignant lesions	**Frequency**	**Percent**
Biphasic Synovial Sarcoma	2	11.1
GIST	1	5.6
Low grade Myxoid sarcoma	2	11.1
Malignant fibrous histiocytoma	3	16.7
Malignant peripheral nerve sheath tumour (MPNST)	1	5.6
Undifferentiated Pleomorphic Sarcoma	8	44.4
Malignant round cell tumour	1	5.6
Total	***18***	***100.0***
Table 10		

DISCUSSION: Although incisional biopsy is the gold standard for the diagnosis of soft tissue masses, reliance on minimally invasive techniques as FNAC to procure diagnostic tissue has become more common and need of the hour.[6]

FNAC has many advantages that make it a first choice diagnostic approach in many tumours. It is an outpatient procedure, it doesn't need anaesthesia and it permits sampling of different parts of a large tumour to evaluate its heterogeneity.[7] Also, properly performed, FNAC is the least tissue invasive diagnostic procedure and risk of sarcoma spread is negligible.[8] On performing FNAC to STT's, five passes should be made with the needle being moved back and forth through the specimen without exiting the skin surface. It is recommended to sample tissue from at least three different parts from the tumour to assess its heterogeneity.[9] FNAC gives reasonably accurate diagnosis of various types of STT, although complex heterogeneity is a challenging factor in the diagnosis of various types of STT.

Our's was a retrospective study of 2 years comprising of 104 cases of either sex, referred from different departments with a clinical suspicion of STT. The aim of the study is to review the role of FNAC in diagnosing soft tissue tumours and to establish cytological criteria for the most encountered STT.

Sex: In our study there was a male preponderance with M: F ratio of 1.08: 1. This is comparable to Chatura et al who also reported male predominance with M: F ratio of 1.25.[10]

Age: Majority of STT in our study were observed in the age group of 21-30 years in case of benign lesions and 41-50 years in case of malignant lesions. Mean age was from 11 days to 75 years. Ahmed et al reported most common age

group for benign tumours in 1st and 5th decade.[11] Nagira et al reported mean age of 48 years, while Bezabih found the most common age group for benign tumours as 4th and 5th decade and for malignant tumours 1st and 2nd decade which is in contrast to our study.[12,13]

Site: Most frequent affected sites were lower limb (n=48) followed by upper limb (n=39). This is in concordance with Nagira et al and Bezabih et al who also found lower extremity to be most common site.

Clinical Presentation: The main clinical presentation was swelling observed in all patients, followed by pain in 20 patients (19.2%). Size of swelling ranged from 0.5×5 cm to 10×20 cm. Majority of the swelling were solitary, multiple lesions were seen in only 6 cases (5.7%) This is similar to Sharanabasav et al who also reported swelling in 100% patients followed by pain in 2.3% cases, with size of swelling ranging from 0.5×5 to 20×20 cm and multiple swelling in 17% cases.[14]

Among 104 soft tissue lesions studied, 86(82.3%) were diagnosed as benign lesions while malignant lesions were reported in 18(17.3%) cases. Ahmed et al reported 83.3% cases as benign and 16.7% cases as malignant.[11] Other authors like Sharanabasav et al also reported benign tumours as 76% and malignant as 16%.[14]

Under benign lesions category, 17(16.3%) cases diagnosed as benign fibrous histiocytoma on FNAC showed loose and tight clusters of oval to spindle cells with minimal pleomorphism and nucleus showed uniformly distributed chromatin, multinucleated giant cells and few histiocytes in the background of collagenous matrix. Soni et al found 11 cases of fibrohistiocytic cases and found solid cell clusters and dispersed spindle shaped cells, thereby giving predominantly a spindle cell smear pattern in cytology smears.[15]

The second most common benign lesion was observed as ganglion cyst 14(13.5%) which on aspiration showed histiocyte like cells in myxoid background and thus findings were similar to the study done by Dodd LG et al who also found thick, gelatinous fluid and a smear comprised of histiocytes embedded in a mucoid matrix.[16]

13 cases (12.5%) were diagnosed as haemangioma. Aspiration yielded only gush of blood and cytology revealed occasional endothelial cells in a haemorrhagic background. The findings were in accordance with study done by Soni et al which found majority of the smears poor in cells and showed blood only.[15]

9 cases (8.7%) were categorized as benign spindle cell lesion. On aspiration, smears showed fragments of loose and tight clusters of oval to spindle cells having uniformly distributed chromatin and minimal pleomorphism. In any aspirate from a spindle cell lesion, the main criteria to be assessed are cellularity, nuclear pleomorphism, mitosis, and necrosis. Aspirates should be carefully evaluated to distinguish a low-grade sarcoma from a benign spindle cell lesion if there is no definite necrosis or any mitosis or clearly pleomorphic nuclei or very high cellularity.[17]

6 cases (5.8%) of neurofibroma were reported. Soft tissue swellings diagnosed as neurofibroma were painful clinically and cytology showed clusters and individually scattered spindle cells with their nucleus showing wavy pointed ends in a background of fibrillary matrix. 5 cases (4.7%) were reported as schwannoma which on aspiration smears showed fragments of spindle shaped cells with pointed wavy ends and fibrillary matrix, abundant intercellular collagen and nuclear palisading. Verocay bodies were evident in 2 cases of schwannoma. Dahl I et al in their study concluded that both schwannomas and neurofibromas show fibrillary background and presence of nuclear palisading or Verocay bodies favours a schwannoma over a neurofibroma.[18]

6(5.8%) cases of GCT were diagnosed and on aspiration showed predominantly multinucleated giant cells along with cells having round to oval nuclei and pale chromatin. Iyer et al found in GCT, the aspirates showing multinucleated giant cells of osteoclastic cell type and two kinds of stromal cells - spindle-shaped cells and polygonal cells with cytoplasm.[19]

6 infants (5.8%) presented with swelling in cervical region and were diagnosed as infantile fibromatosis. Smears showed cluster and scattered oval to spindle cells with moderate pleomorphism, uniformly distributed chromatin and few multinucleated cells. Clinical features such as age, site, and cytological features-bland-appearing fibroblasts, degenerative, atrophic skeletal muscle, and giant cells without inflammatory cells, helps in diagnosis of infantile fibromatosis.[20,21,22]

3 cases (2.9%) were reported as proliferative fasciitis. Smears showed scattered plump spindle cells, ganglion cells in a myxoid background. The nuclear chromatin of these cells were fine and pleomorphism was noted in occasional cells. Nodular fascitis was diagnosed in 3 patients (2.9%). Smears were cellular and showed many individually scattered spindle to plump cells in myxoid background. Mild nuclear atypia and occasional ganglion like cells were also noted. The FNAC features of nodular fasciitis and proliferative fasciitis are mostly same, except that proliferative fasciitis shows lower cellularity, more collagen fragments, and abundant ganglion-like cells.[23]

There were 3 cases (2.9%) reported as lymphangioma. Aspiration yielded clear fluid in all the three cases. Smear showed lymphoid cells in a haemorrhagic background. Orelle et al found that fluid aspirated from a lymphangioma showed cholesterol crystals, lymphoid cells mainly small lymphocytes and endothelial cells.[24]

1 patient (1%) was diagnosed as desmoid fibromatosis who presented with swelling on previous low caesarean section scar. On aspiration, smear showed moderate cellularity comprising of clusters of plump fibroblast entrapped in collagen. Raab et al observed in this lesion, the cell yield comprising of spindled cells, scattered or in clusters, with indistinct cytoplasm and moderate anisokaryosis. Fragments of more or less cellular collagenous tissue as common feature observed.[25]

Malignant Lesions: Out of 104 soft tissue lesions, 18 cases (17.3%) were diagnosed as malignant.

3 cases (2.9%) were reported as malignant fibrous histiocytoma (MFH). FNA showed single as well as clusters of cells showing pleomorphism with large nuclei, coarse clumped chromatin, some with eosinophilic cytoplasm, prominent nucleoli, giant multinucleated cells, atypical mitosis and necrosis. The two main cell types were mono- and multinucleated, large pleomorphic, often bizarre, histiocyte-like cells and atypical fibroblast-like cells. For a correct diagnosis of pleomorphic MFH, it is important to recognize atypical large polymorphic tumor cells which show signs of phagocytosis, cell debris or even well-preserved cells within the tumour cell cytoplasm.[26] The important differential diagnosis of MFH includes anaplastic large cell lymphoma, leiomyosarcoma, pleomorphic liposarcoma, pleomorphic rhabdomyosarcoma. Osama M concluded that the cytologic features of MFH on FNA are not specific and include clusters of atypical polygonal and spindle cells with bizarre, multinucleated giant cells.[27]

Biphasic synovial sarcoma was diagnosed in 2 patients (1.9%). On aspiration, smears were cellular and showed dual population of cells comprising of clusters of spindle shaped cells intermixed with round to polygonal epithelial looking cells with vesicular nuclei, inconspicuous nucleoli and gland like structures. Cytological features show short, uniform spindle and epithelial cells with uniform vesicular nuclei and micronucleoli. Gland formation in biphasic lesions is a useful diagnostic feature.[28]

2 cases (1.9%) were reported as low grade myxoid sarcoma. On aspiration, smear were moderately cellular and showed abundant myxoid material, collagenous stroma, scattered oval to spindle cells with moderate pleomorphism and some cells with large pleomorphic nuclei. Lindberg GM, et al found in their study that low grade fibromyxoid sarcoma is difficult to distinguish from benign myxoid/spindle tumours such as soft tissue perineurioma due to variable cell yield, variable prominent myxoid matrix and slightly atypical spindly or ovoid cells.[29]

One of the patient (1%) presented with swelling scapular region and on aspiration smear were highly cellular and showed dual population of cells arranged in loose cohesive clusters and also singly scattered. One type of cells were small rounded, irregular dark nuclei with scant cytoplasm and other type of cells were large with moderate and fragile cytoplasm and granular chromatin. This was categorized under malignant round cell tumour category and the possibility of Extraskeletal Ewing's sarcoma was extended. However, this tumour is often confused with other round, small-cell neoplasms, including primitive neuroectodermal tumour, neuroblastoma, embryonal rhabdomyosarcoma, and lymphoma.[30]

Eight cases (7.6%) were reported as undifferentiated pleomorphic sarcoma. Smear were highly cellular and showed clusters of pleomorphic cells with many bizarre nuclei, tumour giant cells and necrosis in 7 cases. In the most recent WHO classification of soft tissue tumours, undifferentiated pleomorphic sarcomas are considered part of the morphologic spectrum of all undifferentiated soft tissue sarcomas and is defined as a group of pleomorphic, high-grade sarcomas in which any attempt to disclose their line of differentiation has failed. Microscopically, marked pleomorphism admixed with bizarre giant cells, spindle cells, and variable foamy cells are seen.[31] One case showed low cellularity, however comprising of pleomorphic cells, hyperchromatic nuclei, necrosis with few bizarre cells. In this case possibility of pleomorphic sarcoma was reported.

1(1%) case of malignant peripheral nerve sheath tumour (MPNST) was diagnosed and the smear showed highly cellular smears comprising of sheets and clusters of pleomorphic spindle cells with elongated, wavy nuclei, tumour giant cell, and mitosis. Myxoid substance with vague storiform pattern was also present. Mc Gee et al concluded in their study that cytomorphological features may strongly suggest MPNST and clinical correlation is essential. Immunocytochemistry (S-100 protein) help to distinguish MPNST from other spindle-cell sarcomas. Origin from a pre-existing neurofibroma, or occurrence in a patient with von Recklinghausen's disease, confirms the diagnosis of MPNST.[32]

1(1%) patient was diagnosed with malignant GIST who presented with abdominal mass in epigastric region. Ultrasound guided FNA was done and cytological smears were showed clusters of spindle to oval cells along with epithelial looking cells with moderate amount of cytoplasm, vesicular nuclei, prominent nucleoli and atypical mitosis. The spindle cells had blunt ended nuclei. Vij et al in their study observed mitosis as the key morphologic feature that suggested high grade malignant GIST and concluded that cytology is a useful method for preoperative diagnosis and follow-up of GISTs.[33]

CONCLUSION: Histopathology has always been documented as gold standard in diagnosis of STT. With the availability of ample data on cytological findings in FNA smears of various benign and malignant STT, it can be emphasised that with material being adequate, FNA smears of STT–benign as well as malignant can help us to arrive at a definite diagnosis in majority of cases with no need for histopathology. In certain cases, with overlapping cytological findings, clinical details and various radiological findings can help us to pin point the diagnosis of small round cell tumours.

Limitations of the Study: The adequacy of material and overlapping cytological features still remain a big limitation in arriving at a definite diagnosis on FNA smears only in certain tumours like MFH, low grade myxoid sarcoma, undifferentiated pleomorphic sarcoma, MPNST and GIST and histopathology still remains the gold standard.

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